

Review Article

Formaldehyde-releasers: relationship to formaldehyde contact allergy.

Part 2. Formaldehyde-releasers in clothes: durable press chemical finishes

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This is the second part of a review article on formaldehyde-releasers used as durable press chemical finishes (DPCF) in textiles. The early finishes contained large amounts of free formaldehyde, which led to many cases of allergic contact dermatitis to clothes in the 1950s and 1960s. Currently, most finishes are based on modified dimethylol dihydroxyethyleneurea, which releases less formaldehyde. Nevertheless, recent studies in the United States and Israel have identified patients reacting to DPCF, considered to have allergic contact reactions to clothes, either from formaldehyde released by the DPCF therein or from the DPCF *per se* (in patients negative to formaldehyde). However, all studies had some weaknesses in design or interpretation and in not a single case has the clinical relevance been proven. The amount of free formaldehyde in most garments will likely be below the threshold for the elicitation of dermatitis for all but the most sensitive patients. The amount of free cyclized urea DPCF in clothes is unlikely to be high enough to cause sensitization. Patch test reactions to formaldehyde-releasing DPCF will in most cases represent a reaction to formaldehyde released from the test material.

Key words: contact allergy; durable press chemical finishes; formaldehyde; textile dermatitis. © John Wiley & Sons A/S, 2010.

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This is the second part of a review article on contact allergy to formaldehyde in durable press chemical finishes (DPCF). *Part 1* (1) presented the chemistry of DPCF, legislation in various countries and studies on the amount of formaldehyde present in clothes. In addition, the DPCF that caused contact allergy were presented with CAS, synonyms, molecular formula, chemical structure, applications, and patch test studies. In *part 2* (this article), the frequency of sensitization to DPCF, occupational contact sensitization, relevance of patch test reactions, and relationship to formaldehyde contact allergy are reviewed followed by a discussion of both parts of the article together.

Frequency of Sensitization

The reported frequencies of sensitization to DPCF are summarized in Table 1. There have been only two studies in which all consecutive patients suspected of contact dermatitis have been routinely tested with a series of DPCF, both from the same country (Israel) and the same author and probably overlapping each other (2, 3). In the most recent study of Lazarov in Israel (2), 40 of 644 (6.2%) reacted to one or more of the six DPCF tested. In an earlier small study, the authors found a 5.9% incidence among 286 patients, but this probably included some patients allergic to formaldehyde who did not react to DPCF (3). In studies with *selected* patch testing,

Table 1. Frequency of sensitization to durable press chemical finishes (DPCF)

Country and year	Number tested	Number positive (%)	DPCF tested	Comments	References
<i>Routine testing</i>					
Israel 1999–2002	644	40 (6.2%)	DMDHEU, DDEU, DMDHEU modified, EUMF, MF, UF	–	2
Israel 2001	286	17 (5.9%)	DMDHEU, DMPU, EUMF, MF, UF, TMAD	Of the 17 patients an unknown number were allergic to formaldehyde but not to DPCF	3
<i>Testing in patients with suspected textile allergic contact dermatitis</i>					
USA 1994–1999	188	35 (18.6%)	DMDHEU, DMPU, EUMF, MF, TMAD, UF	The patients were selected for further testing with DPCF, which may have resulted in 'overselection'	8
Israel 1991–1997	55	3 (5.5%)	DMDHEU, DMPU, EUMF, MF, UF	–	9
USA 1988–1991	?	13	DMDHEU, DMPU, EUMF, MF, TMAD, UF	The 13 patients represented 2.8% of the total patch test population of 462. Certain (occupational) groups of patients were excluded from consideration	6
USA 1988–1990	?	16	DMDHEU, DMPU, EUFR, EUMF, MF, TMAD, UF	The 16 patients represented 1.6% of the total patch test population of 1022	7
Denmark 1970–1980	428	15 (3.5%)	DMDHEU, DMMPU, DMPU, EUMF, UF	The 15 patients represented 0.3% of the entire patch test population	5
<i>Frequency of individual DPCF in routine testing (for details see under the individual DPCF)</i>					
		1.7%	1,3-dimethyl-4,5-dihydroxyethyleneurea		
		0.6–2.3%	Dimethylol dihydroxyethyleneurea		
		2.2%	Dimethylol dihydroxyethyleneurea, modified		
		2.1%	Dimethylolpropyleneurea		
		2.0–7.2%	Ethylene urea, melamine/formaldehyde resin		
		2.4–2.6%	Melamine/formaldehyde resin		
		2.3–2.4%	Urea–formaldehyde resin		
		2.4%	Tetramethylol acetylenediurea		

DDEU, 1,3-dimethyl-4,5-dihydroxyethyleneurea; DMDHEU, dimethylol dihydroxyethyleneurea; DMDHEU modified, dimethylol dihydroxyethyleneurea modified; DMMPU, dimethylolmethoxypropylene urea; DMPU, dimethylolpropyleneurea; EUFR, ethylene urea–formaldehyde resin; EUMF, ethylene urea, melamine/formaldehyde; MF, melamine/formaldehyde; TMAD, tetramethylol acetylenediurea; UF, urea–formaldehyde.

the patients diagnosed with textile allergic contact dermatitis represented 1% (4), 0.3% (5), 2.8% (6), and 1.6% (7) of the total patch test population. The percentages positive reactions to DPCF in selected patients obviously depend on the mode of selection and varied from 3.5% to 18.6% (8). Several authors, however, found the same percentage as in their routinely tested patients (9) or a low yield in selected patients (5), which may indicate that clinical suspicion is not sensitive. Individual DPCF routinely tested have yielded positive responses ranging from 0.6% to 7.2%. The latter percentage was an extremely high North American Contact Dermatitis Group (NACDG) prevalence rate for ethylene urea, melamine/formaldehyde (10). The NACD routinely tested this substance since 1994. Prevalence rates in the 1990s ranged from 5.0% to 7.2% (10–12). Since 2001, the rates are stable at a level a little over 2% (13–15) and similar results were obtained by investigators from

the Mayo Clinic (16). Note that ethylene urea, melamine/formaldehyde is a Chemotechnique® mix for patch testing (Chemotechnique Diagnostics®, Vellinge, Sweden), but not a DPCF used as such in clothes. With dimethylol dihydroxyethyleneurea, routine testing yielded low frequencies of positive reactions ranging from 0.2% to 1.1% in all studies (3, 13–15) but one small investigation (2.3%, 17).

Relevance of Positive Patch Test Reactions

Fowler et al. in the United States (7) presented 16 patients reacting to one or more DPCF among 1022 patch test patients (1.6%). He considered all of them to be clinically relevant, the diagnosis of allergic contact dermatitis from clothes appeared to be based solely on positive patch tests to DPCF (7). It was not stated how many patients had been tested with the group of DPCF and whether there had been positive reactions not considered relevant. In an Israeli

group of 83 patients who reacted to colours and/or DPCF, the reactions were considered to be currently relevant in 81% of the cases (not specified for DPCF only (2). In a group of 428 contact dermatitis patients tested in Denmark with a series of textile finish resins because of suspected textile dermatitis, 15 had one or more positive reactions. Ten cases (67%) were considered to be relevant, seven to urea-formaldehyde and three to dimethylolpropyleneurea (5). In a group of 286 Israeli patients tested with a series of colours and DPCF, there was current relevance in 69% of those with one or more positive patch test reactions, but this was not specified for DPCF only (3). Sherertz in the USA found 11 positive reactions to one or more DPCF among 462 patch tested patients and considered all of them to represent clothing reactions (6). Relevance scores for individual DPCF can be found in Tables 5–12 in part 1 of this article (1). There is considerable experience with ethylene urea, melamine/formaldehyde, which is routinely tested by the NACDG in the United States since 1994 [Table 8 (1)]. The positive reactions were considered to have 'definite or probable relevance' in 9–27% of the cases; 'possible' relevance was scored for 29–60% of the reactions (11–13, 15). In two NACDG reports (11, 12), 'definite relevance' was scored separately and represented 1.4% and 7.7% of all reactions. The Mayo Clinic considered 2/3 of all reactions as currently relevant, but without specifications (16). Note that both the members of the NACDG and the Mayo Clinics often function as tertiary referral centres, where many patients are not followed-up after completion of patch testing, which makes establishing relevance problematic. The risk of relevance being overestimated was also indicated by the NACDG itself (12). In no single report have attempts been made to demonstrate the presence of the putative allergen in the clothes worn by the patients, be it formaldehyde or the DPCF *per se*.

Relationship Between Patch Tests to DPCF and Formaldehyde Contact Allergy

There is an obvious relationship between positive patch tests to DPCF and formaldehyde contact allergy, which is expected, as all DPCF available for patch testing, with the exception of 1,3-dimethyl-4,5-dihydroxyethyleneurea (Fixapret® NF, NF = non – formaldehyde), are formaldehyde-releasers. In some studies all patients reacting to DPCF were also allergic to formaldehyde (4, 5, 19). In the other US studies, co-reactions to formaldehyde were observed in 67% (8), 82% (17), 73% (6), and 75% (7) of patients reacting to one or more DPCF, and in 63–100% for individual DPCF (Table 2). Testing with formaldehyde 1% aqua may result

in up to 40% false-negative reactions (20) and we have previously argued that most, if not all, negative reactions to formaldehyde in the US studies may have been false-negative (21). Therefore, it is surprising and unexpected that in the Israeli studies only about one-third of all patients positive to DPCF co-reacted to formaldehyde (2, 3); we have no explanation for this discrepancy and neither have the authors of these publications (A. Lazarov, personal communication, October 2009).

There is less data on the reverse relationship, i.e. how many patients allergic to formaldehyde co-react to DPCF. The 15 patients with allergic contact dermatitis due to formaldehyde in textiles constituted 8.6% of the formaldehyde-allergic patients in an early Danish study (15), but only a minority had been tested with DPCF. Sherertz tested 18 of 63 patients allergic to formaldehyde or formaldehyde-releasers but not suspected of clothing dermatitis with six DPCF; they were all negative (6).

Relationship between DPCF and other DPCF

Most patients reacting to a DPCF are also allergic to other DPCF (if tested). In the US study of Fowler et al. (7) among 1022 patients there were 16 who had one or more positive reactions to a series of DPCF. Together they had 58 positive DPCF patch tests, an average of 3.6 reactions. Four reacted to five, and two patients had even positive patch tests to all six DPCF (7). In an Israeli series of 40 patients allergic to DPCF, there were 82 positive patch tests, a mean of 2.1 reactions per patient (2). In Denmark, five patients allergic to DPCF reacted to on average 2.2 of a series of five DPCF tested (5). In the United States, 188 patients suspected of clothing dermatitis were tested with six DPCF. Of the 24 patients who had at least two positive reactions, eight reacted to all six DPCF and the mean number of positive patch tests was 4.8 (8). Scheman et al. retested 10 US patients known to react to DPCF with a series of 12 DPCF. There were 49 positive patch tests, an average of 4.9 per patient (4).

Relationship between DPCF and other – non-DPCF – formaldehyde-releasers

In the American study of Fowler et al. (7) of 16 patients who reacted to one or more DPCF, 12 (75%) also reacted to the (chemically unrelated) cosmetic formaldehyde-releasers quaternium-15 and/or diazolidinyl urea and/or imidazolidinyl urea and/or DMDM hydantoin. Remarkably, this was also the case in three of four patients that did react to DPCF but were negative to formaldehyde.

Table 2. Relationship between patch tests to durable press chemical finishes (DPCF) and contact allergy to formaldehyde

Country and year	Number of patients tested	DPCF tested	Number positive to DPCF	Number positive to formaldehyde (%)	References
USA 1999–2004	852	EUMF	17	14 (82%)	17
Israel 1999–2002	844	DDEU, DMDHEU (+methylated), EUMF, MF, UF	40	? (34%)	2
Israel 2001 (?)	286	DMDHEU, DMPU, EUMF, MF, TMAD, UF	17 (?)	? (35%)	3
Finland 1991–2001	863	MF	15	15 (100%)	19
USA 1994–1999	188	All together	24 ^a	16 (67%)	8
		DMDHEU	16	12 (75%)	
		DMPU	23	16 (70%)	
		EUMF ^b	11	10 (91%)	
		EUMF ^b	11	7 (64%)	
		MF	18	14 (78%)	
		TMAD	21	16 (76%)	
		UF	16	10 (63%)	
USA 1988–1991	?	All together	11	8 (73%)	6
		DMDHEU	1	1 (100%)	
		DMPU	2	2 (100%)	
		EUMF	1	1 (100%)	
		MF	2	2 (100%)	
		TMAD	1	1 (100%)	
		UF	10	7 (70%)	
USA 1994–1996	3071	EUMF	155	137 (88%)	11
USA 1988–1990	?	All together	16	12 (75%)	7
		DMDHEU	5	5 (100%)	
		DMPU	11	10 (91%)	
		EUMF	14	11 (79%)	
		MF	11	8 (73%)	
		TMAD	8	7 (88%)	
		UF	10	9 (90%)	
Denmark 1970–1980	428	DMDHEU, DMPU, EUMF, MF, UF	15	15 ^c (100%)	5

DDEU, 1,3-dimethyl-4,5-dihydroxyethyleneurea; DMDHEU, dimethylol dihydroxyethyleneurea; DMDHEU modified, dimethylol dihydroxyethyleneurea, modified; DMPU, dimethylolpropyleneurea; EUFR, ethylene urea–formaldehyde resin; EUMF, ethylene urea, melamine/formaldehyde; MF, melamine/formaldehyde; TMAD, tetramethylol acetylenediurea; UF, urea–formaldehyde resin.

^aThere were 11 more patients positive in this group, but they reacted to one DPCF only and their details were not provided.

^bEUMF was tested in duplicate.

^cTested as formaldehyde 2% aqua.

Occupational Contact Allergy to Durable Press Chemical Finishes

Reports of occupational allergic contact dermatitis to DPCF in the textile industry are infrequent in the past 30 years. A US paediatrician developed dermatitis attributed to a hospital gown and a face mask. She was patch tested several times and reacted to formaldehyde, quaternium-15, imidazolidinyl urea, urea–formaldehyde resin, melamine/formaldehyde resin and ethylene urea, melamine/formaldehyde. The presence of formaldehyde in the mask and in one gown was (qualitatively) demonstrated. The manufacturer denied the use of formaldehyde in the mask, but admitted that ‘trace impurities’ could be present (22). Of the 17 patients allergic to ethylene urea, melamine/formaldehyde resin investigated by Carlson et al. in the United States (17), there were six occupational cases: three male retirees and three women, an office worker, a dialysis technician

and a machinist. No details on exposure to the test material (which is a mix of two finishes, and which is not used as such) were provided, but it was suggested that they had become sensitized to formaldehyde first and later cross-reacted to DPCF (which would actually indicate that the reactions to EUMF were *not* relevant) (17). Among 83 Israeli patients reacting to either a DPCF or a colour used in clothes, there were four occupational cases (occupation not specified) (2). A man handling new ready-made clothes in a warehouse had eczema on the hands that improved during weekends and holidays. Patch tests were positive to formaldehyde, quaternium-15, and ethylene urea, melamine/formaldehyde (18). Bracamonte et al. in Spain (23) reported on one (atopic) patient with hand eczema that got worse when replacing clothes in a store. She reacted to formaldehyde and several (high formaldehyde) DPCF. Soni and Sherertz in the United States between 1989 and 1994 investigated

Table 3. Occupational allergic contact dermatitis to melamine/formaldehyde resin

Number of patients	No. allergic to formaldehyde	Occupation/work activities	Responsible products	References
1	0	Melamine paper impregnating line	Melamine/formaldehyde	28
3	0	Compositor in chipboard factory	Melamine/formaldehyde resin coating	19
		Laboratory technician	Melamine/formaldehyde glue	19
		Plywood worker	Melamine/formaldehyde glue	19
5	0	Workers in plant producing resin-fibre composites	Melamine/formaldehyde resin	29
1	?	?	?	30
1	0	Orthopaedic plaster technician	Orthopaedic plaster	31
1	1	Production of clay pots	Gypsum moulds for clay pots	32

19 patients with dermatitis who were occupationally involved with finished textile products. Six were diagnosed as suffering from allergic contact dermatitis to DPCF on the basis of a positive patch test to formaldehyde or a DPCF (24). Between 1975 and 1993, the average annual incidence of formaldehyde-related occupational contact dermatitis in the Finnish Textile and Clothing industries was 0.66/10 000 (25). In the US case series of Fowler et al. (7) there were four cases of occupational contact dermatitis (two garment workers, one printer and one chemical worker) among 16 patients sensitized to DPCF. Gasperini et al. in Italy reported on 62 textile and garment industry workers with allergic contact dermatitis, but not a single case was caused by either formaldehyde or a DPCF (26). Romaguera et al. in Spain ascribed petechial facial dermatitis in a patient working in a textile plant to contact with wool on the basis of a positive patch test reaction to formaldehyde and two high-formaldehyde DPCF (27). There have been several reports of occupational contact dermatitis from melamine/formaldehyde resin, but all outside the textile industry; their details are summarized in Table 3.

Discussion

There can be little doubt that in the 1950s and 1960s many patients have suffered from allergic contact dermatitis caused by formaldehyde in clothes due to the presence of DPCF therein. The use of urea-formaldehyde and melamine/formaldehyde resins to prevent wrinkling lead to amounts of free formaldehyde in the range of 5000–12 000 p.p.m. (0.5–1.2%), which may be expected to be able to either induce sensitization or elicit allergic reactions in individuals presensitized to formaldehyde. Whether at the present time formaldehyde released by DPCF in textiles and/or DPCF themselves are able to cause allergic contact dermatitis (2–4, 6–9, 17) and how often this occurs is unclear. There is limited recently published experience with routine and aimed testing with DPCF. Quite curiously, with

the exception of one center in Israel, all reports have come from the United States. The total number of reported patients with positive patch test reactions to certain DPCF is limited, for example, 1 for dihydroxydimethylolethyleneurea, methylated [possibly false-positive due to Excited Skin Syndrome (ESS)]; 13 for 1,3-dimethyl-4,5-dihydroxyethyleneurea (2 possibly false-positive due to ESS); 14 for dimethylol dihydroxyethyleneurea, modified; 33 for dimethylolpropyleneurea and 46 for tetramethylol acetylenediurea. Some test preparations (tetramethylol acetylenediurea, dimethylolpropyleneurea) have not been available since 1999. But more importantly, all published studies presenting data on patch testing with DPCF appear to have certain weaknesses, some of which have previously been addressed (21) and which makes it difficult to draw firm conclusions. These weaknesses include:

- (1) There are only two studies specifically addressing the subject of textile allergic contact dermatitis, in which an unselected patient population has been tested (2, 3). These were two small studies with 644 respectively 286 patients and from the same centre. It is likely that part of the data in the smaller study (3) was also incorporated in the other (2). In both studies, clinical data were presented for a group of patients reacting to either dyes or DPCF. The DPCF data were not separated and no specifics for individual patients were given.
- (2) Most other studies on DPCF textile dermatitis have been retrospective and only part of the patient population (usually unspecified) had been tested with DPCF.
- (3) Ethylene urea, melamine/formaldehyde has been extensively tested in consecutive patients, notably in the United States by the NACDG and the Mayo Clinic (10–16). The results were given only as numbers and percentages positive and (definite, probable or possible) relevant. No clinical details were provided, it was usually not stated how

many patients also reacted to formaldehyde, and most patients were not followed-up after patch testing, so relevance is likely to be overestimated (12). Also, it is unclear what a positive reaction to ethylene urea, melamine/formaldehyde means. In patients allergic to formaldehyde (in the other US studies in some 64–100% of the patients), it may merely be caused by the formaldehyde released by hydrolysis when the substance enters the water-containing skin. Finally, a positive reaction cannot have direct clinical relevance, as the test substance is a mix for patch testing only and not a DPCF used as such.

- (4) Many patients have had multiple positive patch test reactions to DPCF, the average number ranging from 2.1 (2) to 4.8 (8) and 4.9 (4) per patient and to other allergens such as formaldehyde, formaldehyde-releasers (quaternium-15 (6, 7), imidazolidinyl urea (6) and diazolidinyl urea (7), and dyes (2, 3, 6), to name just a few. In many of such cases false-positive reactions due to the ESS may have occurred [or are extremely likely, (4)], but with some exceptions (6), no author reports having retested the patients to verify the sensitization.
- (5) Although relevance of a positive patch test reaction *sensu stricto* can only be considered as proven, when the putative allergen is known to be present or has been demonstrated in the incriminated objects (in these cases usually garments), in the aforementioned studies no author has tried to establish the presence of formaldehyde (either qualitatively or quantitatively) and/or the incriminated DPCF. Only in one occupational case report was formaldehyde demonstrated in a face mask (although the relevance of this can be questioned) (22).
- (6) In some studies, relevance was assumed or considered proven on the basis of a positive patch test only (7, 17), which is currently considered to be inadequate. In others (6, 8), the clinical picture was an important criterion for making the diagnosis. Textile dermatitis is said 'classically' to conform to a pattern that coincides with places on the skin, where clothing may fit tightly. Common eruption sites include the posterior neck, the upper back, lateral thorax (i.e. anterior and posterior axillary folds), waistband, and flexor surfaces, with relative sparing of the undergarment areas. However, the clinical picture in reports of textile allergic contact dermatitis

has varied widely (33) and has included erythrodermic dermatitis (7) and purpuric contact dermatitis (34). Also, aimed patch testing in patients clinically suspected of textile allergic contact dermatitis often resulted in a low yield of positive patch tests, so the clinical picture is considered not to be a sensitive marker (21) and may, therefore, not be suitable for determining relevance.

- (7) Avoidance of garments containing the putative allergens should result in clearing of the dermatitis or at least considerable improvement. In several studies such data was not provided. Others had vague descriptions such as 'most patients improved' (6) or 'a significant proportion improved' (17). On the other side of the spectrum, in the prospective study from Israel (2), the percentage relevant reactions was over 80% 'as demonstrated by the complete resolution of the allergic contact dermatitis after discontinuing exposure to the incriminated allergens in different garments'. The mean time to complete resolution was 20 days. This result compares extremely favourable to that of other studies; the reasons for this are not known, although the authors have suggested that very intensive counselling may have contributed (A. Lazarov, personal communication, October 2009) (2).
- (8) In all US studies (6–8, 17), formaldehyde was considered to be the allergen when patients reacted both to DPCF and formaldehyde. When the patient did not react to formaldehyde, then the DPCF *per se* was considered to be the allergen responsible for the dermatitis. However, formaldehyde is a 'difficult' allergen, and that testing with 1% formaldehyde (as was performed in all studies) may result in up to 40% false-negative reactions (20). Retesting with formaldehyde 1% or 2% (as has been advised by Rietschel and Fowler (35) and by the Swedish Contact Dermatitis group (21) appears not to have been performed.

Textile allergic contact dermatitis caused by formaldehyde

The threshold level of free formaldehyde in clothes that will produce clinical dermatitis in a formaldehyde-allergic patient is unknown. The experiment of Fisher et al. (36) suggests that dermatitis will be produced only when textiles contain over 750 p.p.m. free formaldehyde. It has previously been argued – albeit based on studies with formaldehyde-releasers in cosmetics – that levels of <200 p.p.m. in textiles should be safe for most

patients allergic to formaldehyde (21). As shown in Table 4 in part 1 of this article (1), in not a single analytical study performed in the forgoing 12 years in the United States (4) (Brookstein D, personal communication, 2008), the Netherlands (37), the European Union (38), Australia (39), New Zealand (40) or Denmark (41) have such levels of free formaldehyde been demonstrated in garments. In many countries, legal upper limits for formaldehyde of 120 p.p.m. or less for clothes have been introduced, there are voluntary restrictions in the United States [AAFA (42)], Europe (43) and internationally (44), the industry has many technological possibilities to lower formaldehyde levels to 100 p.p.m. or even <30 p.p.m., washing usually greatly decreases formaldehyde levels, and the hazards of high-formaldehyde concentrations are well known to the industry. Therefore, we feel that—at least in the countries mentioned above—formaldehyde textile allergic contact dermatitis should be infrequent and occur only—if at all (21)—in those patients who are very sensitive to formaldehyde. It cannot be excluded that in certain countries clothes are worn with high-formaldehyde content, for example, from local factories. This cannot be an explanation for the Israeli data, although, as no more than one-third of the patients were allergic to formaldehyde (2, 3).

Textile allergic contact dermatitis caused by DPCF independent of formaldehyde allergy

In the US studies, a negative reaction to formaldehyde in a patient allergic to DPCF was considered 'proof' of sensitization to the DPCF themselves. As previously argued, in many such cases the reaction to formaldehyde may have been false-negative (21). In favour of this assumption is the following: many patients react to both urea-formaldehyde resin and/or melamine/formaldehyde resin and the cyclic ureas such as (modified) dimethylol dihydroxyethyleneurea. These DPCF have quite different structures. As cross-reactivity is, therefore, unlikely (and this goes for concomitant sensitization too) the logical explanation would be a common constituent, the prime candidate for which is of course formaldehyde. Indeed, we have recently demonstrated (Emeis D, de Groot AC, Brinkmann J, 2009, unpublished) that all DPCF test substances currently available from Chemotechnique® either contain formaldehyde (the aqueous preparations) or release it in the presence of water (the petrolatum test substances), with the (expected) exception of 1,3-dimethyl-4,5-dihydroxyethyleneurea, a non-formaldehyde DPCF. In the two Israeli studies (2, 3), only about 1/3 of all patients with positive patch tests to DPCF

co-reacted to formaldehyde, suggesting that the DPCF can indeed cause contact sensitization per se. However, the presence of the incriminated DPCF in clothes worn by these patients was not established. The cyclized urea derivatives are used—as far as we know—only as textile finishes. This means that the patients with positive patch test reactions to them must have been sensitized by the DPCF-containing clothes themselves. In modern textile technology, the methylol groups of the cyclized urea DPCF cross-link with the hydroxyl (OH) groups of the cellulosic textile fibres to form stable ether bonds. We suspect that after adequate curing, few unreacted DPCF molecules remain in the textiles (45). As these molecules are water-soluble, most residues will be washed away when the textiles are washed after curing in the mill or at home. As DPCF do not seem to be potent sensitizers (there are few cases of occupational contact allergy to them), we feel that it is unlikely that such low levels are capable of sensitizing people from wearing clothes containing the finishes. This, however, leaves the positive reactions in the Israeli study (2) unexplained.

Conclusions

There has been limited published experience with patch testing DPCF in either consecutive contact dermatitis patients or in selected patient groups. All studies had some weaknesses in design or interpretation and in not a single case has the clinical relevance been proven, as no investigator has identified the putative allergens in the incriminated garments. The amount of free formaldehyde in most garments will likely be below the threshold for the elicitation of allergic contact dermatitis for all but the most sensitive patients. The (theoretical) amount of free cyclized urea DPCF in clothes is unlikely to be high enough to cause sensitization from their presence in garments. Present data are inadequate to give advice on the indication for patch testing patients with (a series of) DPCF.

Suggested future research

We suggest that prospective studies be performed with routine testing of a commercial DPCF series. The protocol should include that any positive reaction to a DPCF should be repeated to verify the sensitization. In case of a positive reaction to DPCF, but a negative test to formaldehyde, the DPCF should be retested together with formaldehyde 1% and 2% in water to exclude a false-negative reaction to formaldehyde. Special attention should be paid to clinical relevance. In formaldehyde-positive cases with strong suspicion of textile allergic contact dermatitis, tests should be performed to verify

the presence of formaldehyde in the incriminated garment and quantify the amount. In cases where patients are repeatedly positive to DPCF that are used in textiles only and where they are repeatedly formaldehyde negative, the manufacturer of the clothes should be contacted to enquire about the DPCF used (which, admittedly, will not be easy). Alternatively, the presence of the incriminated allergens could be investigated by HPLC investigation. A second suggested line of investigation is to test the series of DPCF in patients known to be allergic to formaldehyde but who are not suspected of textile allergic contact dermatitis (e.g. in countries with formaldehyde restrictions) to better establish the relationship between contact allergy to DPCF and formaldehyde sensitivity. Ideally, these patients should be patch tested with a dilution series of formaldehyde to determine a possible relationship between the strength of the formaldehyde sensitization and the number of positive patch test reactions to DPCF.

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